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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,456	05/10/2005	Katharine H Dixon	4-32303A	3819

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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/525,456	DIXON ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *17-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 1 to 23 are pending in the instant application.

2) Claims 17 to 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected 9invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 24 January of 2006.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3) Claims 1 to 16 are rejected under 35 U.S.C. § 101 because they are drawn to an invention that is inoperative and that lacks a specific and substantial credible utility in currently available form. The instant claims are drawn to a method of identifying "a compound useful for modulating angiogenesis" which consists of identifying compounds that bind to a putative G protein-coupled receptor identified in the instant specification and the prior art as "HB-954". The assertion in text on pages 1 to 3 of the instant specification that compounds that activate or inhibit the activity of an "HB-954" of the instant invention can be used to modulate angiogenesis appears to be based solely on the fact that it "has an endothelial preferred pattern of expression, and that levels of its mRNA are induced by two distinct proangiogenic pathways, ie. that of sphingosine-1-phosphate SPP sphingosine-1-phosphate and VEGF". The claimed method lacks specific and substantial utility in currently available form for several reasons.

First, one of ordinary skill in the art of receptor biology would not believe that the expression pattern of "HB-954", alone, is sufficient to support a conclusion that it is

involved in angiogenesis. A statement of a specific utility is treated as true if it would be believed to be true by one of ordinary skill in the art given the evidence of record. The Bais et al. publication (NATURE 391 :86-89, 01 Jan. 1998) is being relied upon because it demonstrates the type of evidence that one of ordinary skill would require to support an assertion that a particular G protein-coupled receptor in involved in angiogenesis. This reference has established a nexus between the receptor described therein and angiogenesis by showing that the addition of that receptor to a cell that is normally incapable of angiogenesis the ability to produce an angiogenic response. Unlike the Bais et al. publication, there is no evidence provided by the instant specification that "HB-954" binds to know angiogenesis modulating compounds or that the activation, inhibition, addition to, or removal of "HB-954" from a cell has any effect at all on the angiogenenic activity of that cell. One would certainly not conclude that every protein that "has an endothelial preferred pattern of expression" and/or whose level of expression is increased by the administration of an angiogenic factor is directly involved in the regulation of angiogenesis. Therefore, the instant specification leaves it to the artisan to establish a specific relationship, if any, between "HB-954" and the angiogenic activity of a cell expressing "HB-954". It is a matter of law that an invention must have a specific and substantial utility "in currently available form", which precludes the need for further research, if that research is needed to establish or reasonably confirm a utility for the claimed invention (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)), where the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial

utility", " [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

Second, it is well known in the art of receptor biology that the agonist activation of different G protein-coupled receptors can mediate a variety of different cellular responses, including the activation or inhibition secondary messenger systems. For example, it is old and well known in the art of receptor biology that the agonist activation of a D1 type of dopamine receptor stimulates adenylate cyclase in a cell expressing it, the agonist activation of a D2 type of dopamine receptor inhibits adenylate cyclase, and the agonist activation of a D3 type of dopamine receptor has no effect on adenylate cyclase at all. Therefore, even if there was sufficient evidence that "HB-954" is involved in angiogenesis, the instant specification leaves it to the artisan to engage in the additional experimentation that would be needed to discover whether agonist activation of "HB-954" stimulates angiogenesis, inhibits angiogenesis, or effects some other aspect of this process, such as branching or cellular differentiation. As indicated above, the court has prohibited the need for such addition experimentation when it is needed to identify or establish a specific utility for a claimed invention.

Third, even if one assumes that agonist activation of "HB-954" stimulates angiogenesis, and there is no evidence of record that supports such an assumption, the instant specification does not provide the essential information needed to distinguish between a compound that activates "HB-954", a compound that inhibits the activation of "HB-954", and a compound that simply binds thereto. It is well established in the art

that members of the G protein-coupled receptor family mediate a variety of different effector pathways in response to agonist activation, depending upon the particular receptor and the type of cell in which it is expressed. There is no universal assay for detecting the agonist activation of any and all G protein-coupled receptors. Because an artisan would have to know if a compound that binds to "HB-954" is an agonist or antagonist thereto before that compound could be used for "modulating angiogenesis", that artisan would have to make the substantial inventive contribution of discovering the identity of an effector system that is modulated by "HB-954" and whether that system is stimulated or inhibited by the agonist activation of 'HB-954". Further, before an artisan could identify an antagonist of "HB-954", they would have to make the additional inventive contribution of discovering the identity of at least one natural ligand for "HB-954" wherein that ligand activates "HB-954". Therefore, the facts of record support the conclusion that the claimed method lacks specific and substantial utility in its currently available form.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4) Claims 1 to 16 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

5) Claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims expressly require "a HB-954 ligand". However, the instant specification does not contain an adequate written description of any compound that is capable of binding to "HB-954". In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Not only does the instant specification fail to provide a description of the genus of compounds that would be encompassed by the limitation "HB-954 ligand', it fails to

identify even one species within the genus "by structure, formula, chemical name, or physical properties".

6) Claims 8, 9 and 12 to 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims require one to measure the activity of an "HB-954" polypeptide. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that :

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

As indicated above, G protein-coupled receptors are known to activate or inhibit a variety of effector systems in a cell, depending on the particular receptor and the particular cell type in which that receptor is expressed. Because the instant specification has not identified a specific cellular activity that has been shown to be

stimulated or inhibited by the activation of "HB-954", an artisan can not predict, by resort to known scientific law which, if any, of the activities listed in claims 12 to 16 of the instant application are going to be associated with the activation of "HB-954". Therefore, the instant specification leaves it to the artisan to engage in the undue experimentation that would be needed to identify a compound that binds to "HB-954" and then to determine if that binding effects any one or more of the activities listed in the instant claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7) Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd.

App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 2 recites the broad recitation "within a K_D range of $10e^{-6}$ to $10e^{-13}$ "and the claim also recites "preferable within a K_D range of $10e^{-8}$ to $10e^{-12}$ " which is the narrower statement of the range/limitation. Further, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JOHN ULM
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